



Review article

Evidence-based treatments for low sexual desire in women



Lori A. Brotto

University of British Columbia, Department of Obstetrics and Gynaecology, Canada

ARTICLE INFO

Article history:

Received 2 February 2017
 Received in revised form 14 February 2017
 Accepted 16 February 2017
 Available online 22 February 2017

Keywords:

Sexual desire
 Sexual dysfunction
 Sexual interest/arousal disorder
 Flibanserin
 Cognitive behavioral therapy
 Mindfulness

ABSTRACT

Low sexual desire is the most common sexual complaint in women, with multinational studies finding that at least a third of women experience low sexual desire. No single etiology for the development of Female Sexual Interest/Arousal Disorder, the diagnosis laid out by the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders, has been established. There has been considerable interest in pharmacological approaches to improving low desire, and agents targeting a range of neurotransmitters have been examined. To date, only flibanserin, a centrally acting medication targeting the serotonin, dopamine, and norepinephrine systems, has been approved by the Food and Drug Administration (FDA). Despite statistically significant effects on sexual desire, sexual distress, and sexually satisfying events, side-effects are significant, and flibanserin is completely contraindicated with alcohol. As such, there has been renewed interest in advancing the science of psychological approaches to low desire, including cognitive behavioral and mindfulness therapies.

© 2017 Elsevier Inc. All rights reserved.

Contents

1. Low sexual desire in women: Prevalence, predictors, and points of controversy	11
2. Overview of treatment approaches	12
2.1. Pharmacologic treatments of female sexual difficulties	12
2.2. Flibanserin: A breakthrough for female sexual dysfunction?	13
2.3. Psychological treatments for sexual desire difficulties in women: Methodological challenges	13
2.4. Psychological treatments for sexual desire difficulties in women: Cognitive behavioral approaches	14
2.5. Psychological treatments for sexual desire difficulties in women: Mindfulness-based approaches	14
2.6. Predictors of positive responses to treatment	15
2.7. Is combination therapy the wave of the future?	15
2.8. Online therapies for low sexual desire	15
3. Conclusion	16
References	16

1. Low sexual desire in women: Prevalence, predictors, and points of controversy

Though there is a strong societal perception that sex is a universally desired and experienced activity, national probability data indicate high rates of sexual dysfunction in both men and women. Low sexual desire is the most common sexual complaint in women across the life cycle, with representative studies carried out across

a variety of countries finding that at least a third of women experience low sexual desire lasting several months over the past year. When one factors in the co-occurrence of clinically significant distress, these prevalence rates drop, yet remain significant at approximately 7–10% of women reporting a sexual dysfunction (Mitchell et al., 2013; Shifren et al., 2008).

Given that up to 40% of women report difficulties with loss of sexual desire when assessed cross-sectionally at a given point in time, it is critically important to determine whether those symptoms evoke clinically significant distress, and are thus associated

E-mail address: lori.brotto@vch.ca

with a sexual dysfunction, or whether they are transient and adaptive changes to the particular context or situational factors in the woman's life at the time (Mitchell et al., 2013; Witting et al., 2008). As such, the criterion of clinically significant distress is required in order to diagnose a prolonged reduction in, or loss of, sexual desire into a sexual dysfunction.

A diagnosis of a sexual desire dysfunction has historically been guided by criteria set out in the Diagnostic and Statistical Manual of Mental Disorders (DSM). From 1980 until 2013, a diagnosis of Hypoactive Sexual Desire Disorder (HSDD) depended on the symptom of absent or reduced desire for sexual activity and lack of sexual fantasies, with associated clinically significant distress. The DSM-5 (American Psychiatric Association, 2013) introduced polythetic criteria to the diagnosis, in recognition of the varied ways in which women experience sexual desire (and sexual desire problems) (Brotto et al., 2009; Meana, 2010; Nowosielski et al., 2016; Sand and Fisher, 2007). Moreover, duration and severity criteria were introduced into the diagnosis of Sexual Interest/Arousal Disorder (SIAD) in the DSM-5 (American Psychiatric Association, 2013), with a diagnosis made when a woman experiences three of the following for a period of at least six months: (1) reduced or absent desire for sex, (2) reduced or absent sexual thoughts/fantasies, (3) reduced or absent initiation and receptivity of sexual activity, (4) reduced or absent sexual pleasure, (5) reduced desire triggered by sexual stimuli, and/or (6) reduced or absent genital or nongenital sensations. In addition to the persistence of these symptoms, the woman must experience clinically significant distress, and the symptoms must not be attributable to severe relationship distress, significant stress, the effects of a substance, medication, another medical condition, or another non-sexual mental disorder. The scientific and clinical community have engaged in a lively debate about the merits and pitfalls of this revised diagnosis (Balon and Clayton, 2014; Basson, 2014; Clayton et al., 2012a; DeRogatis et al., 2011; Graham et al., 2014; Leckman and Pine, 2012; Sungur and Gündüz, 2014). Critics have argued that polythetic criteria introduce too much heterogeneity into the diagnosis, resulting in women with the same diagnosis having markedly different symptom profiles. On the other hand, comprehensive reviews of the literature demonstrate that women express and experience their sexual desire and arousal in vastly different ways (Meana, 2010; Nowosielski et al., 2016), thereby suggesting that polythetic criteria may be warranted. Furthermore, critics believe that the symptom duration criteria of 6 months unnecessarily raise the bar for reaching a diagnosis, and lead to women with subthreshold criteria without access to needed care (Balon and Clayton, 2015; Clayton et al., 2012a, 2012b). On the other hand, studies that do not impose these symptom severity or duration criteria lead to prevalence rates suggesting that half of women have a sexual dysfunction (Laumann et al., 1999), and may encourage providers to inadvertently administer treatment when the symptoms may reflect a transient and adaptive response to a particular life context.

The causes of low sexual desire in women have been studied at length, and no single etiology for the development of Female Sexual Interest/Arousal Disorder (SIAD) has been established (Brotto et al., 2016a). There has been considerable interest in the role of hormones in the development of low desire (Davis et al., 2004). In particular, the cessation of ovarian production of estrogen with menopause was assumed to trigger the onset of a sexual dysfunction, and contributed to a societal belief that sexual desire dwindled with age in women. Comprehensive, longitudinal, and methodologically rigorous research from around the world, but in particular from Melbourne, Australia, found that whereas the decline in estrogen was associated with vaginal dryness and discomfort, it was not directly associated with a loss of sexual desire (Dennerstein et al., 1999, 2002, 2006; Dennerstein and Leher,

2004). The hormone, testosterone, has also been of tremendous interest given a vast amount of literature in non-human animals demonstrating the impact of testosterone removal on sexual behavior (Beach, 1967), clinical conditions, such as hypogonadism, which is often associated with loss of sexual desire (Hintikka et al., 2009; Weisinger and Bellorin-Font, 2004), and the observation of an ovulatory peak in sexual desire, around the time when testosterone is elevated (Schreiner-Engel et al., 1981). However, studies that have directly compared women with and without sexual desire difficulties have failed to find significant differences in testosterone levels (Basson et al., 2015, 2010; Reed et al., 2016), regardless of whether testosterone was assessed with mass spectrometry, saliva, or other methodologies. Nonetheless, testosterone is a popular form of therapy among some health care providers, as will be discussed in a later section.

2. Overview of treatment approaches

Before the approval and blockbuster success of the oral phosphodiesterase type 5 inhibitor, sildenafil citrate (Viagra), for men with sexual dysfunction, most of the published literature on treatments for women's sexual dysfunction focused on non-pharmacological approaches (Phillips, 2000). William Masters and Virginia Johnson are considered by most to be the pioneers of sex therapy, and their intensive, inpatient program viewed sexual problems through the lens of the couple (Masters and Johnson, 1970). As a result, their treatment, which was largely focused on sensate focus therapy, required participation of both members of the couple. Sensate focus consisted of specific, systematic touching by one person of the other, with early stages prohibiting any breast or genital touch, and subsequent stages including them. While the giver of the touch used their own curiosity to guide where and how they touched, the receiver was instructed to pay attention to the sensations of touch while relaxing. Both partners were instructed that the goal was not pleasure-oriented or to obtain arousal, but rather, to tune into the touch, and to provide the partner verbal and non-verbal feedback about the touch. Their outcomes were remarkable, with 95% of couples responding positively to treatment, and an extremely low remission rate when couples were assessed five years later (Hawton et al., 1991; Hawton, 1995; LoPiccolo and Stock, 1986). Adaptations of the inpatient sensate focus program to an outpatient setting were similarly effective, and thus spurred the genesis of countless sex therapy clinics around North America. For approximately two decades, sex therapy and sensate focus were the predominant clinical approach to treating sexual problems (Perelman, 2014).

2.1. Pharmacologic treatments of female sexual difficulties

Following the approval of Viagra, there was a rapid and marked pendulum shift, with sex researchers increasingly turning their attention to pharmacological approaches for women's sexual dysfunction. This was fueled by considerable funding support from pharmaceutical companies to study the causes of sexual dysfunction in women, and, in parallel, to investigate a plethora of pharmacological treatments (Rowland, 2007). Viagra was tested in a variety of different populations of women (women with spinal cord injury, with multiple sclerosis, those with antidepressant-associated sexual dysfunction, those with mixed etiologies, etc.) and overall, the findings were not consistently impressive, with Viagra being no more effective than placebo in the majority (with a few exceptions being the study for women with spinal cord injury and multiple sclerosis) (Basson and Brotto, 2003; DasGupta et al., 2004; Leddy et al., 2012; Nurnberg et al., 2008). In the end, Pfizer halted its support for studies on women's sexual

functioning (Major, 2004) and experts purported that the targets of sildenafil (i.e., increasing genital engorgement) may not correspond with the source of women's sexual difficulties (Chivers and Rosen, 2010)—the latter being largely based on the brain

Topical testosterone also received a fair share of attention (Nappi et al., 2010; Wierman et al., 2010), and a variety of formulations and administration routes were studied in pre- and postmenopausal women with HSDD. Though the findings were promising, with most showing a statistically significant improvement in sexual desire compared to placebo in estrogen replete women (Achilli et al., 2017), the FDA rejected applications to approve the testosterone patch for women's low sexual desire. Concerns about long-term safety underlined its rejection by the FDA (Moynihan, 2004). Nonetheless, testosterone remains commonly prescribed off-label to this day.

In addition to sildenafil and testosterone, a large number of centrally acting pharmaceuticals have been evaluated in the treatment of low sexual desire in women (Farmer et al., 2016; Parish and Hahn, 2016). These included: the dopamine-norepinephrine reuptake inhibitor and antidepressant, bupropion, which was found to improve sexual desire in depressed and nondepressed women; the melanocortin agonist, bremelanotide, which showed improvements in sexual desire after subcutaneous injection; and various topical agents. More recently, the company Emotional Brain has combined centrally acting with peripherally acting agents as a means to addressing concurrent processes involved in female sexual desire. Lybrido combines sublingual testosterone and sildenafil and Lybridos combines testosterone with bupropion. Both agents were found to improve sexual desire, however, only among those women who displayed sexual inhibition at baseline (Bloemers et al., 2013; Poels et al., 2013), which the authors defined as low sensitivity to sexual cues (van der Made et al., 2009). Before the experimental testing, the participants took part in an Emotional Stroop Test to measure preconscious bias for sexual cues, and their results to this test sorted them into the low sensitivity versus high sensitivity groups. Women in the low sensitivity group also showed an increase in preconscious attention to sexual cues following the medication, as well as a significant increase in genital sexual response to a sexual fantasy, whereas this effect was not found in the "high sensitive to cues" women. Though promising, to date, none of these medications have received FDA approval, but continue to be intensely studied.

2.2. Flibanserin: A breakthrough for female sexual dysfunction?

The landscape shifted on June 4, 2015, when an advisory committee to the FDA voted 18-6 in favor of approving flibanserin for the treatment of low desire in women. Two months later, on August 18, 2015, the FDA approved flibanserin (Addyi), and two months after that, on October 17, 2015, Addyi was available for prescription in the United States. Two meta-analyses reviewing the available literature on flibanserin produced conflicting findings. The first reviewed four published clinical trials of flibanserin based on $n = 3414$ women (Gao et al., 2015) and found statistically greater increases in sexually satisfying events, sexual desire, overall sexual function, and significant reductions in sex-related distress compared with placebo. A second meta-analysis based on five studies, including unpublished randomized controlled trials, demonstrated a less optimistic picture, showing that flibanserin led to a mean increase of only 0.5 sexually satisfying events per month as well as clinically significant risk of dizziness, somnolence, nausea, and fatigue (Jaspers et al., 2016). The conflicting findings in these two meta-analyses further fueled the debate associated with the nature of and optimal treatment for low desire in women. More recently, a third meta-analysis of flibanserin studies has been published (Sahebkar et al., 2016) based on six published

and four unpublished studies on a total of 8345 women. This analysis concluded that although flibanserin was associated with significant increases in sexual desire, the magnitude of this increase did not differ from the effect of placebo (Sahebkar et al., 2016). If prescribing patterns are any indication of its popularity, flibanserin is not likely to make monumental shifts in improving sexual desire for women given that only a few hundred prescriptions were made for flibanserin during the same period of time that a half million prescriptions for Viagra (sildenafil) were written for men (Edney and Colby, 2015). It is possible that flibanserin's complete contraindication with alcohol (due to the finding that it potentiates the risk for dizziness, hypotension, and syncope) for the entire duration of its use may be contributing to the lack of uptake (Fugh-Berman, 2016). What is remarkable about the (unpublished) study of alcohol interactions with flibanserin is that it was based on 23 men and only 2 women (Summary Review for Regulatory Action, 2015), highlighting, for some, the ongoing gender-based biases in sex research.

2.3. Psychological treatments for sexual desire difficulties in women: Methodological challenges

In very recent years, the pendulum seems to have shifted again towards a renewed interest in evaluating psychological treatments for female sexual dysfunction, though there is recognition that judging the effectiveness of psychological therapies in treating sexual problems is inherently more complex than pharmaceutical trials (Chivers et al., 2017; Graham, 2007). Psychological therapies seek not only to ameliorate sexual problems, but also to address broader domains of relationship functioning and quality of life (Meana et al., 2014). Linear models of sexual response such as the human sexual response cycle (Masters and Johnson, 1966), which provided the foundation for diagnosing HSDD for three decades, have been criticized as inadequate to capture the complexity and variability of women (and men's) sexual experiences (Tiefer, 2001). Circular models of sexual response, instead, de-emphasize the primacy of genital response, and instead, also emphasize the role of relationship factors and intimacy, both as motivations for engaging in sexual activity as well as outcomes of a satisfying sexual encounter (Basson, 2000; Kaschak and Tiefer, 2001). A comparison of models in large samples of women reveals that no single model of sexual response captures women's sexual experiences (Giraldo et al., 2015; Nowosielski et al., 2016).

In line with this, there is recognition that in assessing treatment outcome we need to shift the focus from an emphasis on sexual "functioning" (e.g., frequency and intensity of desire and orgasms) to broader and more clinically meaningful outcomes such as sexual satisfaction (Stulhofer et al., 2010), sexual quality of life, and sexual esteem (Abraham et al., 2009). These constructs are multidimensional and hence more challenging to assess than sexual function criteria (Rowland, 2007), but often represent the targets, and measured outcomes in sex therapy settings (Meana et al., 2014).

In recent years, researchers have focused on trying to better understand how women define sexual satisfaction (Pascoal et al., 2014), to develop new measures of sexual satisfaction (Stulhofer et al., 2010), and to compare existing assessment tools (Mark et al., 2014) in how they capture the nuances of sexual experiences. As Meana noted, "we can always target . . . the individual's and couple's level of adjustment to circumstances and the ways in which they process their problem and their relationship dynamics." (Meana et al., 2014, p. 547).

A key challenge in evaluating psychological treatments is how we best define treatment "success", given that more often than not the specific "dysfunction" is only one aspect of the sexual relationship and therapy can sometimes result in improved communication and relationship satisfaction, without any resolution of the

“dysfunction” (Bancroft, 2009). Furthermore, sexual problems are not always associated with sexual dissatisfaction or distress (Ferenidou et al., 2008), and may reflect adaptive, short-term changes. In studies of women, many variables beyond sexual function e.g., psychological wellbeing, relationship adjustment (Dundon and Rellini, 2010) predict sexual satisfaction.

Sexual desire is difficult to define and difficult to measure. Does one count sexual frequencies of various sexual behaviors or attempt to assess the degree of internal motivation to engage in sexual activity? Do we tally sexual fantasies or frequency of various sexual behaviors as a proxy measure of desire or interest? And, perhaps more importantly, what should be considered indicative of a successful treatment outcome? It should be noted that most pharmaceutical trials have focused on “sexually satisfying events” as the primary endpoint, at the recommendation of the FDA, despite the finding that these endpoints do not consistently correlate with women’s self-reported desire or distress (Kingsberg and Althof, 2011).

Basson (2001a) has argued that many women never report spontaneous desire yet can become readily aroused with effective stimulation or the wish to be intimate with a partner. Basson (2001a) postulated that many women in established relationships engage in sex from an initial stance of sexual neutrality and then, with increasing amounts of arousal, begin to experience desire. Often, desire is triggered by a variety of internal motivations or external reinforcements rather than intrinsic physical tension although for women in new relationships, desire may be experienced more spontaneously. It must be acknowledged that the motivations or incentives to either initiate or respond to a sexual request or overture are extremely varied, and may fall into either an approach-related (i.e., reasons for sex to achieve some desired outcome) or avoidance-related (i.e., reasons for sex to avoid some undesired outcome) (Impett et al., 2008). More recently, this research has found that engaging in sex for strictly avoidance-related reasons can be harmful in the long-term (Day et al., 2015). Unfortunately, these key domains of sexual motivation are never measured in treatment-outcome studies. Obviously, knowing that a sexual experience has occurred tells us nothing about either the desire accompanying it, or the diverse and not necessarily sexual motives for engaging in it, and it is possible that a woman may agree to sex for such avoidance-related reasons.

Even in evaluating sexual “function” variables, what constitutes a satisfactory outcome is not always clear. The clinical trials leading to the approval of flibanserin focused on “sexually satisfying events” (Derogatis et al., 2012) with a comparison of frequency count between the arms as an endpoint. Changes in the quality of women’s desire (or sexual encounters) was not reported on. The focus on quantity rather than quality of sexual activity has been heavily criticized given that the change may not be clinically meaningful (Brotto et al., 2010).

The challenges inherent in designing and conducting outcome studies of psychological interventions to treat low sexual desire in women are real, and not likely to go away, particularly with the rise in integrated medical and psychological approaches and if prognostic indicators are identified (Bancroft, 2009). Despite these challenges, it is imperative that methodologically sound outcome studies are carried out in this area.

2.4. Psychological treatments for sexual desire difficulties in women: Cognitive behavioral approaches

Nearly 30 years ago, Hawton (1992) questioned whether sex therapy outcome research had “withered on the vine.” Surprisingly, although experts described cognitive behavioral sex therapy in 1980 (Perelman, 1980), and many sex therapists rely on cognitive behavioral therapy (CBT) in their management of sexual com-

plaints, there have been very few controlled studies evaluating CBT for women’s sexual desire complaints. An exception to the scarcity of treatment outcome studies evaluating CBT for women is in the area of sexual pain disorders, where there have been a number of well-designed controlled outcome studies demonstrating the short and long-term efficacy of CBT for the symptom of genital pain intensity and associated psychological domains (Bergeron et al., 2016, 2008; Ter Kuile et al., 2013).

Because sexual difficulties are associated with cognitive distraction, and negative or biased thoughts during sexual activity (Peixoto and Nobre, 2015), and negative affect (Peixoto and Nobre, 2016), CBT is ideally suited to address these domains of sexual desire in women. Distraction may contribute to women’s difficulties noticing sexual sensations in their bodies, and interfere with responsive desire that often emerges following sexual arousal (Basson, 2001b) because they are not attending to their emerging sexual arousal, and/or judging their own responses negatively.

Two meta-analyses have reviewed the controlled outcome literature on CBT for women with low sexual desire (Frühauf et al., 2013; Günzler and Berner, 2012). A much larger literature exists on uncontrolled studies of CBT for HSDD, however, they are not reviewed here given the strong placebo response in this area of study, and the finding that expectations for a positive response to treatment may interact with treatment efficacy to produce positive outcomes (Boot et al., 2013).

There is a dearth of controlled efficacy data on the psychological treatment of sexual desire disorders, despite the fact that hypoactive sexual desire is the most common female sexual complaint (Mitchell et al., 2013; Shifren et al., 2008). Since the early period of evaluating Masters and Johnson-type therapies based on sensate focus, there have not been many well-controlled studies evaluating psychological therapies for sexual dysfunction. A meta-analysis by Frühauf and colleagues (Frühauf et al., 2013) yielded a total of 20 studies that included a wait-list control group, and another 8 studies that included head-to-head comparisons with other therapies. The cognitive behavioral approaches for women with low desire, which, in general, included behavioral skill training to improve communication between partners, increase sexual skills and reduce sexual and performance anxiety; anxiety reduction, and cognitive challenging were evaluated. The meta-analysis found an overall effect size of $d = 0.91$ for the primary endpoint of low desire in women with HSDD, corresponding to a large effect size. CBT also had a moderate effect on improving sexual satisfaction, $d = 0.51$ in this population. CBT approaches improve other domains of function in addition to the primary endpoint of sexual desire (e.g., quality of sexual and marital life, sexual satisfaction, perception of sexual arousal, sexual self-esteem, depression, and anxiety), and improvements in sexual desire appear to persist up to a year following treatment (Trudel et al., 2001). Another systematic review of this literature also found that inclusion of the male partner in CBT treatment for low desire yielded better outcomes (Günzler and Berner, 2012). CBT remains a widely used treatment for women with low sexual desire, and is recommended at a Grade B level by the 2015 International Consultation on Sexual Medicine (Brotto et al., 2016a).

2.5. Psychological treatments for sexual desire difficulties in women: Mindfulness-based approaches

Mindfulness, a secular practice derived from Buddhist traditions of meditation, involves the practice of observing one’s present-moment thoughts, emotions, and bodily sensations in a non-judgmental manner (Bishop et al., 2004). Through mindfulness training, women with low desire may become more aware of the physical changes they experience during or in anticipation of sexual activity (e.g., genital vasocongestion, tingling), which

may boost and maintain their subjective sexual arousal and desire. Mindfulness training may also target the myriad negative judgments women with sexual difficulties have about themselves (Nobre and Pinto-Gouveia, 2006a, 2006b) as they consider their distressing situation characterized by absent, highly infrequent and/or unsatisfying sexual activity. Though the mechanisms by which mindfulness may impact sexual desire in women have not been thoroughly studied, there is some evidence that it may impact interoceptive awareness, or women's ability to detect and observe bodily sensations (Brotto et al., 2016b; Paterson et al., 2016).

Over the past decade, a collaborative of clinician researchers in sexual medicine, psychology, and mindfulness have worked together to develop and test a group mindfulness-based intervention for women with low sexual desire. Of note, most of the research in this area is based on uncontrolled research, so the previously mentioned concerns about expectancy effects cannot be ruled out when considering this literature. Early research was focused on a three or four session intervention, and revealed improvements in sexual functioning for survivors of gynecologic cancer (Brotto et al., 2008a,b; Brotto et al., 2012a), women seeking treatment for heterogeneous sexual desire and arousal concerns (Brotto and Basson, 2014; Brotto et al., 2008a), and women with a history of childhood sexual abuse (Brotto et al., 2012b). Even when administered to women seeking treatment for chronic vulvodynia, mindfulness led to significant improvements in their level of sexual desire (Brotto et al., 2013, 2015).

Consistent feedback from women was that they requested more sessions of longer duration. We therefore expanded the four to an eight-session intervention, and modelled the in-session mindfulness exercises largely after those utilized in Mindfulness-Based Cognitive Therapy for Depression (MBCT) (Segal et al., 2002). At least one hour in each of the eight weekly sessions was spent guiding participants through a mindfulness exercise, followed by an in-depth inquiry during which they were asked to reflect on how focusing on a particular target (be it a raisin, their breath, their body sensations, sounds, or thoughts) might be relevant to their concerns with low sexual desire. Women were also encouraged to practice mindfulness sessions at home on a daily basis.

In a recent study of 39 women meeting criteria for SIAD (Paterson et al., 2016), compared to pre-treatment, women experienced statistically significant improvements in sexual desire, overall sexual function, sex-related distress, sexual arousal, orgasm, and satisfaction. Improvements in sexual desire showed a very large effect size. Various domains of interoceptive awareness, including, non-distracting, attention regulation, self-regulation, and body-listening also significantly improved, as did mood and rumination. In an analysis of mediators, the study found that improvements in interoception mediated the improvements seen in sexual desire. In other words, it is possible that women's ability to notice and tune into physical sensations, including sexual ones, directly contributed to increasing their level of sexual desire. Mood was also found to be a mediator, however it mediated improvements in overall sexual functioning, not sexual desire specifically.

Though there has been an impressive body of research devoted to adapting and testing mindfulness-based therapies for women with sexual concerns, it remains to be seen how such an approach compares to other established treatments.

2.6. Predictors of positive responses to treatment

Why and how do individuals respond to treatment is of great interest to clinicians as well as researchers. In the domain of treatment for sexual dysfunction, some (Frühauf et al., 2013; Hawton, 1995) have identified a variety of factors that appear to be related to better outcomes with psychological treatment interventions.

These include: the motivation for success of both partners, relationship satisfaction and compliance with homework assignments. Conversely, four variables have been identified with treatment dropout: (1) lower socio-economic status, (2) the male partner's lower or lack of motivation for treatment, (3) a conflicted partner relationship and (4) poor progress by the third treatment session. In general, treatments delivered in a couple and group setting are more effective for the primary symptom endpoint than when applied to individuals, and for sexual satisfaction, it appears that treatment delivered in groups is the most effective format.

2.7. Is combination therapy the wave of the future?

Even in the context of vast growth of female sexual medicine, few would argue that psychological approaches are no longer relevant; indeed, some have suggested that the predominance of sexual medicine and of pharmacological treatments has highlighted the need for an integration of medical and psychological approaches (Rosen et al., 2014). Now that there is an approved medication for the treatment of low desire in women, this may pave the way for combination studies, in which the efficacy of psychological versus pharmaceutical treatments versus their combination may be directly compared. Combination therapy has been purported for many years to have the potential to significantly advance the manner in which men, women and couples receive treatment for sexual dysfunctions (Althof, 1998, 2006; McCarthy, 1998; Perelman, 2005; Rosen, 2000). Combining medical and psychological interventions harnesses the power of both treatments to enhance efficacy, increase treatment and relational satisfaction, and decrease discontinuation with treatment. In other domains of health care (e.g., depression, anxiety, post-traumatic stress disorder), combination therapy is quite readily employed (Andrews et al., 1991).

Combination or integrated treatment is a natural extension of the biopsychosocial model. It addresses the relevant biological, medical, psychological, and social contributors to a sexual concern, as well addressing factors that predispose, precipitate and perpetuate sexual dysfunction. Where sexual pharmaceuticals may be criticized for focusing narrowly or mechanistically at sexual function, and psychological interventions alone may be time consuming, costly and fail to yield rapid symptom amelioration, combination approaches may be superior to either treatment alone.

An emerging body of evidence strongly supports the value of combination treatment although certain issues require further study. For example, (1) What is the best theoretical model for combination therapy? (2) Who delivers the care (nurse, social worker, psychologist, or, physician)? (3) Where is the intervention performed (medical clinic vs. mental health office)? and, (4) Are the medical and psychological treatments concomitant or stepwise (Althof, 2006)? These questions remain to be investigated in future combination studies for women's low sexual desire.

2.8. Online therapies for low sexual desire

A recent Cochrane review indicated a positive effect of bibliotherapy for sexual dysfunction, however, mostly small studies of low quality provide limited evidence (van Lankveld et al., 2006). No significant differences were found between interventions that did versus those that did not provide adjuncts to the online therapy. Moreover, none of the studies reported on acceptability of the intervention or adherence to treatment requirements. More large, high-quality, comparison studies using online modalities are needed (van Lankveld, 2016; van Lankveld et al., 2006).

3. Conclusion

Our understanding of the factors that contribute to sexual desire as well as to development of a sexual desire difficulty, remain poorly understood. What is clear, however, is that a sizable proportion of women across ages and reproductive and life stages are dissatisfied with their sexual desire. As advances in the science of understanding women's sexual desire continue to evolve, we hope that there is a concomitant increase in the science evaluating treatments. There is an urgent need for developing better control groups in psychological treatment outcome studies given that psychological expectancies can bolster outcomes, and because there may be non-specific factors unassociated with a particular treatment modality that contribute to improved sexual desire. There is also hope that both sides of the age-long debate over the nature of women's desire can come together in a collaborative effort to understand and improve women's experiences.

References

- Abraham, L., Symonds, T., May, K., Althof, S.E., Hallam-Jones, R., Rosen, R.C., 2009. Psychometric validation of gender nonspecific sexual confidence and sexual relationship scales in men and women. *J. Sex. Med.* 6, 2244–2254.
- Achilli, C., Pundir, J., Ramanathan, P., Sabatini, L., Hamoda, H., Panay, N., 2017. Efficacy and safety of transdermal testosterone in postmenopausal women with hypoactive sexual desire disorder: a systematic review and meta-analysis. *Fertil. Steril.* 107 (2), 475–482.
- Althof, S., 1998. New roles for mental health clinicians in the treatment of erectile dysfunction. *J. Sex. Educ. Therapy* 23, 229–231.
- Althof, S., 2006. Sex therapy in the age of pharmacotherapy. *Ann. Rev. Sex Res.* 17, 116–132.
- American Psychiatric Association, 2013. *Diagnostic and Statistical Manual of Mental Disorders*. American Psychiatric Association, Washington, DC.
- Andrews, F.M., Abbey, A., Halman, L.J., 1991. Stress from infertility, marriage factors, and subjective well-being of wives and husbands. *J. Health Soc. Behav.* 32 (3), 238–253.
- Balon, R., Clayton, A.H., 2014. Female sexual interest/arousal disorder: a diagnosis out of thin air. *Arch. Sex. Behav.* 43 (7), 1227–1229.
- Balon, R.S., Clayton, A., 2015. Further commentary on DSM-5 FSIAD diagnosis. *J. Sex. Med.* 2 (2), 576–577.
- Bancroft, J., 2009. *Human Sexuality and its Problems*. Churchill Livingstone, Edinburgh.
- Basson, R., 2014. On the definition of female sexual interest/arousal disorder. *Arch. Sex. Behav.* 43 (7), 1225–1226.
- Basson, R., Young, A., Brotto, L.A., Driscoll, M., Corrie, S., Labrie, F., 2015. Is there a correlation between androgen and sexual desire in women? Letter to the editor. *J. Sex. Med.* 12 (7), 1654–1655.
- Basson, R., 2000. The female sexual response: a different model. *J. Sex Marital Ther.* 26 (1), 51–65.
- Basson, R., 2001a. Human sex-response cycles. *J. Sex Marital Ther.* 27 (1), 33–43.
- Basson, R., 2001b. Using a different model for female sexual response to address women's problematic low sexual desire. *J. Sex Marital Ther.* 27 (5), 395–403.
- Basson, R., Brotto, L.A., 2003. Sexual psychophysiology and effects of sildenafil citrate in oestrogenised women with acquired genital arousal disorder and impaired orgasm: a randomised controlled trial. *BJOG: Int. J. Obstet. Gynaecol.* 110 (11), 1014–1024.
- Basson, R., Brotto, L.A., Petkau, J.A., Labrie, F., 2010. Role of androgens in women's sexual dysfunction. *Menopause* 17 (5), 962–971.
- Beach, F.A., 1967. Cerebral and hormonal control of reflexive mechanisms involved in copulatory behavior. *Physiol. Rev.* 47 (4), 289–316.
- Bergeron, S., Khalifé, S., Dupuis, M.J., McDuff, P., 2016. A randomized clinical trial comparing group cognitive-behavioral therapy and a topical steroid for women with dyspareunia. *J. Consult. Clin. Psychol.* 84 (3), 259–268.
- Bergeron, S., Khalifé, S., Glazer, H.I., Binik, Y.M., 2008. Surgical and behavioral treatments for vestibulodynia: two-and-one-half year follow-up and predictors of outcome. *Obstet. Gynecol.* 111 (1), 159–166.
- Bishop, S.R., Lau, M., Shapiro, S., Carlson, L., Anderson, N.D., Carmody, J., 2004. Mindfulness: a proposed operational definition. *Clin. Psychol.: Sci. Pract.* 11 (3), 230–241.
- Bloemers, J., van Rooij, K., Poels, S., Goldstein, I., Everaerd, W., Koppeschaar, H., et al., 2013. Toward personalized sexual medicine (part 1): integrating the "dual control model" into differential drug treatments for hypoactive sexual desire disorder and female sexual arousal disorder. *J. Sex. Med.* 10 (3), 791–809.
- Boot, W.R., Simons, D.J., Stothart, C., Stutts, C., 2013. The pervasive problem with placebos in psychology: why active control groups are not sufficient to rule out placebo effects. *Perspect. Psychol. Sci.* 8 (4), 445–454.
- Brotto, L., Atallah, S., Johnson-Agbakwu, C., Rosenbaum, T., Abdo, C., Byers, S., et al., 2016a. Psychological and interpersonal dimensions of sexual function and dysfunction. *J. Sex. Med.* 13, 538–571.
- Brotto, L.A., Basson, R., 2014. Group mindfulness-based therapy significantly improves sexual desire in women. *Behav. Res. Ther.* 57, 43–54.
- Brotto, L.A., Basson, R., Carlson, M., Zhu, C., 2013. Impact of an integrated mindfulness and cognitive behavioural treatment for provoked vestibulodynia (IMPROVED): a qualitative study. *Sex. Relat. Ther.* 28 (1–2), 3–19.
- Brotto, L.A., Basson, R., Luria, M., 2008a. A mindfulness-based group psychoeducational intervention targeting sexual arousal disorder in women. *J. Sex. Med.* 5 (7), 1646–1659.
- Brotto, L.A., Basson, R., Smith, K.B., Driscoll, M., Sadownik, L., 2015. Mindfulness-based cognitive therapy for women with provoked vestibulodynia. *Mindfulness* 6, 417–432.
- Brotto, L.A., Bitzer, J., Laan, E., Leiblum, S., Luria, M., 2010. Women's sexual desire and arousal disorders. *J. Sex. Med.* 7 (1), 586–614.
- Brotto, L.A., Chivers, M.L., Millman, R.D., Albert, A., 2016b. Mindfulness-based sex therapy improves genital-subjective arousal concordance in women with sexual desire/arousal difficulties. *Arch. Sex. Behav.* 45 (8), 1907–1921. <http://dx.doi.org/10.1007/s10508-015-0689-8>.
- Brotto, L.A., Erskine, Y., Carey, M., Ehlen, T., Finalyson, S., Heywood, M., et al., 2012a. A brief mindfulness-based cognitive behavioral intervention improves sexual functioning versus wait-list control in women treated for gynecologic cancer. *Gynecol. Oncol.* 125 (2), 320–325.
- Brotto, L.A., Heiman, J.R., Goff, B., Greer, B., Lentz, G.M., Swisher, E., et al., 2008b. A psychoeducational intervention for sexual dysfunction in women with gynecologic cancer. *Arch. Sex. Behav.* 37 (2), 317–329.
- Brotto, L.A., Heiman, J.R., Tolman, D.L., 2009. Narratives of desire in mid-age women with and without arousal difficulties. *J. Sex Res.* 46 (5), 387–398.
- Brotto, L.A., Seal, B.N., Rellini, A., 2012b. Pilot study of a brief cognitive behavioral versus mindfulness-based intervention for women with sexual distress and a history of childhood sexual abuse. *J. Sex Marital Ther.* 38 (1), 1–27.
- Chivers, M., Basson, R., Brotto, L.A., Graham, C.A., Stephenson, K.R., 2017. Statistical and epistemological issues in the evaluation of treatment efficacy of pharmaceutical, psychological, and combination treatments for women's sexual desire difficulties. *J. Sex Marital Ther.* Advance online publication <http://dx.doi.org/10.1080/0092623X.2016.1266538>.
- Chivers, M.L., Rosen, R.C., 2010. Phosphodiesterase type 5 inhibitors and female sexual response: faulty protocols or paradigms? *J. Sex. Med.* 7 (2), 858–872.
- Clayton, A.H., DeRogatis, L.R., Rosen, R.C., Pyke, R., 2012a. Intended or unintended consequences? The likely implications of raising the bar for sexual dysfunction diagnosis in the proposed DSM-V revisions: 1. For women with incomplete loss of desire or sexual receptivity. *J. Sex. Med.* 9 (8), 2027–2039.
- Clayton, A.H., DeRogatis, L.R., Rosen, R.C., Pyke, R., 2012b. Intended or unintended consequences? The likely implications of raising the bar for sexual dysfunction diagnosis in the proposed DSM-V revisions: 2. For women with loss of subjective sexual arousal. *J. Sex. Med.* 9 (8), 2040–2046.
- DasGupta, R., Wiseman, O.J., Kanabar, G., Fowler, C.J., 2004. Efficacy of sildenafil in the treatment of female sexual dysfunction due to multiple sclerosis. *J. Urol.* 171 (3), 1189–1193.
- Davis, S.R., Guay, A.T., Shifren, J.L., Mazer, N.A., 2004. Endocrine aspects of female sexual dysfunction. *J. Sex. Med.* 1 (1), 82–86.
- Day, L.C., Muise, A., Joel, S., Impett, E.A., 2015. To do it or not to do it? How communally motivated people navigate sexual interdependence dilemmas. *Pers. Soc. Psychol. Bull.* 41 (6), 791–804.
- Dennerstein, L., Koochaki, P., Barton, I., Graziottin, A., 2006. Hypoactive sexual desire disorder in menopausal women: a survey of western European women. *J. Sex. Med.* 3 (2), 212–222.
- Dennerstein, L., Leher, P., 2004. Modeling mid-aged women's sexual functioning: a prospective, population-based study. *J. Sex Marital Ther.* 30 (3), 173–183.
- Dennerstein, L., Leher, P., Burger, H., Dudley, E., 1999. Factors affecting sexual functioning of women in the mid-life years. *Climacteric* 2 (4), 254–262.
- Dennerstein, L., Randolph, J., Taffe, J., Dudley, E., Burger, H., 2002. Hormones, mood, sexuality, and the menopausal transition. *Fertil. Steril.* 77 (Suppl. 4), S42–S48.
- DeRogatis, L.R., Clayton, A.H., Rosen, R.C., Sand, M., Pyke, R.E., 2011. Should sexual desire and arousal disorders in women be merged? *Arch. Sex. Behav.* 40, 217–219.
- Derogatis, L.R., Komer, L., Katz, M., Moreau, M., Kimura, T., Garcia, M., et al., 2012. Treatment of hypoactive sexual desire disorder in premenopausal women: efficacy of flibanserin in the VIOLET study. *J. Sex. Med.* 9 (4), 1074–1085.
- Dundon, C.M., Rellini, A.H., 2010. More than sexual function: predictors of sexual satisfaction in a sample of women age 40–70. *J. Sex. Med.* 7, 896–904.
- Edney, A., Colby, L., 2015. Valeant's newest problem: the female libido pill isn't selling. *The Globe and Mail*. Retrieved from <<http://www.theglobeandmail.com/report-on-business/valeants-newest-problem-the-female-libido-pill-isnt-selling/article27291467/>>
- Farmer, M., Yoon, H., Goldstein, I., 2016. Future targets for female sexual dysfunction. *J. Sex. Med.* 13 (8), 1147–1165.
- Ferenidou, F., Kapoteli, V., Moisisdis, K., Koutsogiannis, I., Giakoumelos, A., Hatzichristou, D., 2008. Presence of a sexual problem may not affect women's satisfaction from their sexual function. *J. Sex. Med.* 5, 631–639.
- Frühau, S., Gerger, H., Schmidt, H.M., Munder, T., Barth, J., 2013. Efficacy of psychological interventions for sexual dysfunction: a systematic review and meta-analysis. *Arch. Sex. Behav.* 42 (6), 915–933.
- Fugh-Berman, A., 2016. Advice against flibanserin. *Am. J. Nurs.* 116, 13.
- Gao, Z., Yang, D., Yu, L., Cui, Y., 2015. Efficacy and safety of flibanserin in women with hypoactive sexual desire disorder: a systematic review and meta-analysis. *J. Sex. Med.* 12 (11), 2095–2104.

- Giraldi, A., Kristensen, E., Sand, M., 2015. Endorsement of models describing sexual response of men and women with a sexual partner: an online survey in a population sample of Danish adults ages 20–65 years. *J. Sex. Med.* 12 (1), 116–128.
- Graham, C.A., 2007. Medicalization of women's sexual problems: a different story? *J. Sex Marital Ther.* 33, 443–447.
- Graham, C.A., Brotto, L.A., Zucker, K.J., 2014. Response to Balon and Clayton (2014): female sexual Interest/Arousal disorder is a diagnosis more on firm ground than thin air. *Arch. Sex. Behav.* 43 (7), 1231–1234.
- Günzler, C., Berner, M.M., 2012. Efficacy of psychosocial interventions in men and women with sexual dysfunctions – a systematic review of controlled clinical trials: Part 2 – the efficacy of psychosocial interventions for female sexual dysfunction. *J. Sex. Med.* 9 (12), 3108–3125.
- Hawton, K., 1992. Sex therapy research: has it withered on the vine? *Ann. Rev. Sex Res.* 3, 49–72.
- Hawton, K., 1995. Treatment of sexual dysfunctions by sex therapy and other approaches. *Br. J. Psychiatry* 167 ((E-11)), 307–314.
- Hawton, K., Catalan, J., Fagg, J., 1991. Low sexual desire: sex therapy results and prognostic factors. *Behav. Res. Ther.* 29 (3), 217–224.
- Hintikka, J., Niskanen, L., Koivumaa-Honkanen, H., Tolmunen, T., Honkalampi, K., Lehto, S.M., et al., 2009. Hypogonadism, decreased sexual desire, and long-term depression in middle-aged men. *J. Sex. Med.* 6 (7), 2049–2057.
- Impett, E.A., Strachman, A., Finkel, E.J., Gable, S.L., 2008. Maintaining sexual desire in intimate relationships: the importance of approach goals. *J. Pers. Soc. Psychol.* 94 (5), 808–823.
- Jaspers, L., Feys, F., Bramer, W.M., Franco, O.H., Leusink, P., Laan, E.T., 2016. Efficacy and safety of flibanserin for the treatment of hypoactive sexual desire disorder in women: a systematic review and meta-analysis. *JAMA Internal Med.* 176 (4), 453–462.
- Kaschak, E., Tiefer, L. (Eds.), 2001. *A New View of Women's Sexual Problems*. Haworth Press, New York, NY.
- Kingsberg, S.A., Althof, S.E., 2011. Satisfying sexual events as outcome measures in clinical trials of female sexual dysfunction. *J. Sex. Med.* 8, 3262–3270.
- Laumann, E.O., Paik, A., Rosen, R.C., 1999. Sexual dysfunction in the United States: prevalence and predictors. *J. Am. Med. Assoc.* 281 (6), 537–544.
- Leckman, J.F., Pine, D.S., 2012. Editorial commentary: challenges and potential of DSM-5 and ICD-11 revisions. *J. Child Psychol. Psychiatry* 53 (5), 449–453.
- Leddy, L.S., Yang, C.C., Stuckey, B.G., Sudworth, M., Haughie, S., Sultana, S., et al., 2012. Influence of sildenafil on genital engorgement in women with female sexual arousal disorder. *J. Sex. Med.* 9 (10), 2693–2697.
- LoPiccolo, J., Stock, W.E., 1986. Treatment of sexual dysfunction. *J. Consult. Clin. Psychol.* 54 (2), 158–167.
- Major, S., 2004. Pfizer will not apply for a license for sildenafil for women. *Br. Med. J.* 328, 542.
- Mark, K.P., Herbenick, D., Fortenberry, J.D., Sanders, S., Reece, M., 2014. A psychometric comparison of three scales and a single-item measure to assess sexual satisfaction. *J. Sex Res.* 51, 159–169.
- Masters, W.H., Johnson, V.E., 1966. *Human Sexual Response*. Little, Brown, Boston, MA.
- Masters, W.H., Johnson, V.E., 1970. *Human Sexual Inadequacy*. Little, Brown, Boston, MA.
- McCarthy, B.W., 1998. Integrating Viagra into cognitive-behavioral couples sex therapy. *J. Sex Educ. Ther.* 23 (3), 302–308.
- Meana, M., Hall, K.S.K., Binik, Y.M., 2014. Sex therapy in transition: Are we there yet? In: Binik, M., Hall, K.S.K. (Eds.), *Principles and Practice of Sex Therapy*. fifth ed. Guilford, New York, NY, pp. 541–557.
- Meana, M., 2010. Elucidating women's (hetero) sexual desire: definitional challenges and content expansion. *J. Sex Res.* 47 (2), 104–122.
- Mitchell, K.R., Mercer, C.H., Ploubidis, G.B., Jones, K.G., Datta, J., Field, N., et al., 2013. Sexual function in Britain: findings from the third national survey of sexual attitudes and lifestyles (Natsal-3). *The Lancet* 382, 1817–1829.
- Moynihan, R., 2004. FDA panel rejects testosterone patch for women on safety grounds. *Br. Med. J.* 329 (7479), 1363.
- Nappi, R.E., Albani, F., Santamaria, V., Tonani, S., Martini, E., Terreno, E., et al., 2010. Menopause and sexual desire: the role of testosterone. *Menopause Int.* 16, 162–168.
- Nobre, P., Pinto-Gouveia, J., 2006a. Dysfunctional sexual beliefs as vulnerability factors for sexual dysfunction. *J. Sex Res.* 43 (1), 68–75.
- Nobre, P., Pinto-Gouveia, J., 2006b. Emotions during sexual activity: differences between sexually functional and dysfunctional men and women. *Arch. Sex. Behav.* 35 (4), 491–499.
- Nowosielski, K., Wróbel, B., Kowalczyk, R., 2016. Women's endorsement of models of sexual response: correlates and predictors. *Arch. Sex. Behav.* 45 (2), 291–302.
- Nurnberg, H.G., Hensley, P.L., Heiman, J.R., Croft, H.A., Debattista, C., Paine, S., 2008. Sildenafil treatment of women with antidepressant-associated sexual dysfunction: a randomized controlled trial. *J. Am. Med. Assoc.* 300 (4), 395–404.
- Parish, S.J., Hahn, S.R., 2016. Hypoactive sexual desire disorder: a review of epidemiology, biopsychology, diagnosis, and treatment. *Sex. Med. Rev.* 4 (2), 103–120.
- Pascoal, P.M., Narciso, I.D.S.B., Pereira, N.M., 2014. What is sexual satisfaction? Thematic analysis of lay people's definitions. *J. Sex Res.* 51, 22–30.
- Paterson, L.Q.P., Handy, A., Brotto, L.A., 2016. A pilot study of 8-session mindfulness-based cognitive therapy adapted for women's sexual interest/arousal disorder. *J. Sex Res.* Advance online publication. <[http://onlinelibrary.wiley.com/journal/10.1111/\(ISSN\)1743-6109](http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1743-6109)>.
- Peixoto, M.M., Nobre, P., 2015. Cognitive schemas activated in sexual context: a comparative study with homosexual and heterosexual men and women, with and without sexual problems. *Cognitive Ther. Res.* 39 (3), 390–402.
- Peixoto, M.M., Nobre, P., 2016. Positive and negative affect during sexual activity: differences between homosexual and heterosexual men and women, with and without sexual problems. *J. Sex Marital Ther.* 42 (1), 4–17.
- Perelman, M., 1980. Treatment of premature ejaculation. In: Leiblum, S.R., Pervin, L.A. (Eds.), *Principles and Practice of Sex Therapy*. Tavistock, London, UK, pp. 199–233.
- Perelman, M., 2005. Combination therapy for sexual dysfunction: integrating sex therapy and pharmacotherapy. In: Balon, R., Segraves, R. (Eds.), *Handbook of Sexual Dysfunction*. Taylor and Francis, New York, pp. 13–41.
- Perelman, M.A., 2014. The history of sexual medicine. In: Tolman, D.L., Diamond, L.M. (Eds.), *APA handbook of sexuality & psychology: Volume 2. Contextual approaches*. American Psychological Association, pp. 137–179.
- Phillips, N.A., 2000. Female sexual dysfunction: evaluation and treatment. *Am. Fam. Physician* 61 (1), 127–136.
- Poels, S., Bloemers, J., van Rooij, K., Goldstein, I., Gerritsen, J., van Ham, D., et al., 2013. Toward personalized sexual medicine (part 2): testosterone combined with a PDE5 inhibitor increases sexual satisfaction in women with HSDD and FSAD, and a low sensitive system for sexual cues. *J. Sex. Med.* 10 (3), 810–823.
- Reed, B.C., Bou Nemer, L., Carr, B.R., 2016. Has testosterone passed the test in premenopausal women with low libido? A systematic review. *Int. J. Women's Health* 8, 599–607.
- Rosen, N.O., Bergeron, S., Sadikaj, G., Glowacka, M., Baxter, M.L., Delisle, I., 2014. Relationship satisfaction moderates the associations between male partner responses and depression in women with vulvodynia: a dyadic daily experience study. *Pain* 155 (7), 1374–1383.
- Rosen, R., 2000. Medical and psychological interventions for erectile dysfunction: toward a combined treatment. In: Leiblum, S., Rosen, R. (Eds.), *Principles and Practices of Sex Therapy*. third ed. Guilford Press, New York.
- Rowland, D.L., 2007. Will medical solutions to sexual problems make sexological care and science obsolete? *J. Sex Marital Ther.* 33 (5), 385–397.
- Sahebkar, A., Saadat, S.H., Panahi, Y., Kabir, A., Rahmani, K., Hosseinalhashemi, M., 2016. Systematic review and meta-analysis of flibanserin's effects and adverse events in women with hypoactive sexual desire disorder. *Curr. Drug Metab. Advance online publication*. <<http://benthamscience.com/journals/current-drug-metabolism/>>
- Sand, M., Fisher, W.A., 2007. Women's endorsement of models of female sexual response: the nurses' sexuality study. *J. Sex. Med.* 4 (3), 708–719.
- Schreiner-Engel, P., Schiavi, R.C., Smith, H.J., White, D., 1981. Sexual arousability and the menstrual cycle. *Psychosom. Med.* 43 (3), 199–214.
- Segal, Z.V., Williams, J.M.G., Teasdale, J.D., 2002. *Mindfulness-Based Cognitive Therapy for Depression: A New Approach to Preventing Relapse*. Guilford Press, New York, NY.
- Shifren, J.L., Monz, B.U., Russo, P.A., Segreti, A., Johannes, C.B., 2008. Sexual problems and distress in United States women: prevalence and correlates. *Obstet. Gynecol.* 112 (5), 970–978.
- Stulhofer, A., Busko, V., Brouillard, P., 2010. Development and bicultural validation of the new sexual satisfaction scale. *J. Sex Res.* 47, 257–268.
- Summary Review for Regulatory Action, 2015. Center for Drug Evaluation and Research <http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/022526REMS.pdf> (accessed February 14, 2017).
- Sungur, M.Z., Gündüz, A., 2014. A comparison of DSM-IV-TR and DSM-5 definitions for sexual dysfunctions: critiques and challenges. *J. Sex. Med.* 11, 364–373.
- Ter Kuile, M.M., Melles, R., de Groot, H.E., Tuijnman-Raasveld, C.C., van Lankveld, J.J., 2013. Therapist-aided exposure for women with lifelong vaginismus: a randomized waiting-list control trial of efficacy. *J. Consult. Clin. Psychol.* 81, 1127–1136.
- Tiefer, L., 2001. A new view of women's sexual problems: Why new? Why now? *J. Sex Res.* 38 (2), 89–96.
- Trudel, G., Marchand, A., Ravart, M., Aubin, S., Turgeon, L., Fortier, P., 2001. The effect of a cognitive-behavioral group treatment program on hypoactive sexual desire in women. *Sex. Relat. Ther.* 16 (2), 145–164.
- van der Made, F., Bloemers, J., Yassem, W.E., Kleiverda, G., Everaerd, W., van Ham, D., Oliver, B., Koppeschaar, H., Tuiten, A., 2009. The influence of testosterone combined with a PDE5-inhibitor on cognitive, affective, and physiological sexual functioning in women suffering from sexual dysfunction. *J. Sex. Med.* 6, 777–790.
- van Lankveld, J.J.D.M., 2016. Internet-based interventions for women's sexual dysfunction. *Curr. Sex. Health Rep.* 8, 136–143.
- van Lankveld, J.J.D.M., Hunot, V., Wylie, K., 2006. Bibliotherapy for sexual dysfunction (protocol). *Cochrane Database Syst. Rev.* 4 (CD006238), 1–8.
- Weisinger, J.R., Bellorin-Font, E., 2004. Outcomes associated with hypogonadism in women with chronic kidney disease. *Adv. Chronic Kidney Dis.* 11 (4), 361–370.
- Wierman, M.E., Nappi, R.E., Avis, N., Davis, S.R., Labrie, F., Rosner, W., et al., 2010. Endocrine aspects of women's sexual function. *J. Sex. Med.* 7 (1 Pt 2), 561–585.
- Witting, K., Santtala, P., Varjonen, M., Jern, P., Johansson, A., von der Pahlen, B., et al., 2008. Female sexual dysfunction, sexual distress, and compatibility with partner. *J. Sex. Med.* 5 (11), 2587–2599.